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EXAMINER	
CARTER, KENDRA D	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/787,071	DUDLEY, ROBERT E.	
	Examiner	Art Unit	
	Kendra D. Carter	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *1-31,51 and 52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III, claims 32-50, in the reply filed on July 24, 2007 is acknowledged. The traversal is on the ground(s) that given that the Examiner has categorized each Group in the same class and subclass, the search and examination of the claims will not cause undue burden. This is not found persuasive because while the searches may be overlapping there is no reason to believe that the searches would be co-extensive. For instance, in Group IV, the Examiner will be focusing on the patentability of the product itself, and not the processes of using of Groups I-III. Conversely, in searching Groups I-III, the Examiner will be focusing on the patentability of the processes and not the product itself. Accordingly, a search for both groups would pose an undue burden on the Office.

Claims 1-31 and 51-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups, there being no allowable generic or linking claim.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 39 recites the limitation "lower alcohol" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 43 and 44 recite the limitation "thickener" in line 1 of claim 43 and line 2 of claim 44. There is insufficient antecedent basis for this limitation in the claim.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(1) Claims 32, 39-42, 45, 46 and 50 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 13, 14, 22-30, 35, 36, 37, 39, 52, 58, 60 and 64 of copending Application No. 10/825,540 in view of Reed et al. (US 6,299,900 B1).

This is a provisional obviousness-type double patenting rejection.

The Application 140,825,540 ('540) teaches a method of treating hypogonadism in a male subject, comprising applying gel containing testosterone to skin of a male subject, wherein the application results in a steady-state testosterone 24-hour pharmacokinetic profile in the male subject (see claims 1, 6 and 35). The application causes improved sexual performance and increase in the percentage of full erection by the male subject (see claims 13 and 14). The gel comprises testosterone, penetration enhancer and 40% to 90% w/w of a C1-C4 alcohol comprising at least one of ethanol, 2-propanol, n-propanol and mixtures thereof (see claims 23, 35, 36 and 64). The testosterone is present from about 0.1% to about 10% w/w, about 0.5% to about 5% w/w, or 1% w/w (see claims 22-26 and 58). The testosterone may be derivatives (see claim 27) The penetration enhancer is isopropyl myristate in a concentration of about 0.1% to about 5% w/w, or about 0.5% (see claims 28-30, 37, 39 and 60).

Application '540 does not specifically teach a method for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction.

Reed et al. teach a precutaneous or transdermal drug delivery system comprising at least one physiologically active agent such as testosterone (see column 14, line 59), at least one volatile liquid such as ethanol (see column 11, line 21) and a penetration enhancer such as isopropyl myristate (see column 10, lines 63 and 64 and abstract, lines 1-10). Reed et al. teaches that some major problems with the current state of the art relate to a lack of efficacy of systemic drugs because of the low drug flux across the skin (see column 1, lines 28-31). Transdermal systemic drug delivery provides an effective method of achieving improved bioavailability for physiologically active substances where the drugs are poorly absorbed by traditional routs of delivery (see column 1, lines 48-51).

One of ordinary skill in the art would have found it obvious to combine '540 and the specific method for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction because Reed et al. teaches that a lack of efficacy of systemic drugs because of the low drug flux across the skin (see column 1, lines 28-31), and transdermal systemic drug delivery provides an effective method of achieving improved bioavailability for physiologically active substances (see column 1, lines 48-51). Thus, by delivering the drug through a drug delivery system of Reed et al. will increase penetration of the drug through the skin and thus improve the efficacy.

(2) Claims 32, 39-42, 45-46 and 50 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 13, 14, 22-30, 35-37, 39, 40, and 44-47 of copending Application No. 10/828,678 in view of Reed et al. (US 6,299,900 B1).

This is a provisional obviousness-type double patenting rejection.

The Application 10,828,678 ('678) teaches a method of treating hypogonadism in a male subject, comprising applying gel containing testosterone to skin of a male subject, wherein the application results in a steady-state testosterone 24-hour pharmacokinetic profile in the male subject (see claims 1, 6 and 35). The application causes improved sexual performance and increase in the percentage of full erection by the male subject (see claims 13 and 14). The gel comprises testosterone, penetration enhancer and 40% to 90% w/w of a C1-C4 alcohol comprising at least one of ethanol, 2-propanol, n-propanol and mixtures thereof (see claims 22, 23, 35 and 36). The testosterone is present from about 0.1% to about 10% w/w, about 0.5% to about 5% w/w, or 1% w/w (see claims 22-26 and 44-47). The testosterone may be derivatives (see claim 27) The penetration enhancer is isopropyl myristate in a concentration of about 0.1% to about 5% w/w, or about 0.5% (see claims 28-30, 37, 39 and 60).

Application '678 does not specifically teach a method for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction.

Reed et al. teach a precutaneous or transdermal drug delivery system comprising at least one physiologically active agent such as testosterone (see column 14, line 59), at least one volatile liquid such as ethanol (see column 11, line 21) and a penetration enhancer such as isopropyl myristate (see column 10, lines 63 and 64 and abstract, lines 1-10). Reed et al. teaches that some major problems with the current state of the art relate to a lack of efficacy of systemic drugs because of the low drug flux across the skin (see column 1, lines 28-31). Transdermal systemic drug delivery provides an effective method of achieving improved bioavailability for physiologically active substances where the drugs are poorly absorbed by traditional routs of delivery (see column 1, lines 48-51).

One of ordinary skill in the art would have found it obvious to combine '678 and the specific method for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction because Reed et al. teaches that a lack of efficacy of systemic drugs because of the low drug flux across the skin (see column 1, lines 28-31), and transdermal systemic drug delivery provides an effective method of achieving improved bioavailability for physiologically active substances (see column 1, lines 48-51). Thus, by delivering the drug through a drug delivery system of Reed et al. will increase penetration of the drug through the skin and thus improve the efficacy.

(3) Claims 32, 40-42, 45 and 47are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 33, 38, 46, 58, 67-69, 70 and 73 of copending Application No. 10/828,678 in view of Reed et al. (US 6,299,900 B1).

This is a provisional obviousness-type double patenting rejection.

The Application 10,828,678 ('678) teaches a method of treating hypogonadism in a male subject, comprising administering a pharmaceutical composition daily, wherein the testosterone is absorbed into bloodstream of the subject at a rate and duration that maintains a circulating serum concentration (i.e. steady state; see claims 33 and 58). The composition comprises from about 0.1% to about 10% w/w or from about 0.5% to about 5% w/w or 1% w/w of testosterone, a penetration enhancer and 40% to 90% of an alcohol (see claims 33, 67, 68 and 73). The penetration enhancer is isopropyl myristate in a concentration of about 0.25 to about 2.5% w/w, or about 0.5% (see claims 69 and 70).

Application '678 does not specifically teach a method for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction.

Reed et al. teach a precutaneous or transdermal drug delivery system comprising at least one physiologically active agent such as testosterone (see column 14, line 59), at least one volatile liquid such as ethanol (see column 11, line 21) and a penetration enhancer such as isopropyl myristate (see column 10, lines 63 and 64 and abstract, lines 1-10). Reed et al. teaches that some major problems with the current state of the art relate to a lack of efficacy of systemic drugs because of the low drug flux across the skin (see column 1, lines 28-31). Transdermal systemic drug delivery provides an effective method of achieving improved bioavailability for physiologically active substances where the drugs are poorly absorbed by traditional routs of delivery (see column 1, lines 48-51).

One of ordinary skill in the art would have found it obvious to combine '678 and the specific method for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction because first, it is known within the art that testosterone is a pharmaceutical drug used to treat erectile dysfunction. Second, Reed et al. teaches that a lack of efficacy of systemic drugs because of the low drug flux across the skin (see column 1, lines 28-31), and transdermal systemic drug delivery provides an effective method of achieving improved bioavailability for physiologically active substances (see column 1, lines 48-51). Thus, by delivering the drug through a drug delivery system of Reed et al. will increase penetration of the drug through the skin and thus improve the efficacy.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

(1) Claims 32, 37-45, 47 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reed et al. (US 6,299,900 B1) in view of Dittgen et al. (US 6,238,284 B1), in further view of Kim et al. (US 5,482,970).

Reed et al. teach a precutaneous or transdermal drug delivery system for humans (see abstract, lines 1-15) comprising at least one physiologically active agent such as papaverine (see column 5, line 31; addresses claim 35), alprostadil (see claim 21), phentolamine (see column 5, line 31; addresses claim 35), or preferably testosterone (see column 14, line 59 and claim 21; addresses claims 32, 40, 41, and

49), at least one volatile liquid such as ethanol (see column 11, line 21; addresses claims 32, 39 and 44) and a penetration enhancer such as oleic acid (column 10, line 58; addresses claims 37 and 38) or isopropyl myristate (see column 10, lines 63 and 64 and abstract, lines 1-10; addresses claims 32, 40, 42 and 44). Reed et al. teaches that some major problems with the current state of the art relate to a lack of efficacy of systemic drugs because of the low drug flux across the skin (see column 1, lines 28-31; addresses claim 32). Transdermal systemic drug delivery provides an effective method of achieving improved bioavailability for physiologically active substances where the drugs are poorly absorbed by traditional routes of delivery (see column 1, lines 48-51; addresses claim 32). The isopropyl myristate and ethanol may be used in range of 1 to 50%. Because of the effect of the penetration enhancer, the dosage of the physiologically active agent may often be less than that conventionally used. The concentration of physiologically active agents used in the drug delivery system will depend on its properties and may be equivalent to that normally utilized for the particular agent in conventional formulations. Both the amount of the physiologically active agent and the amount of penetration enhancer will be influenced by the type of effect desired (see column 11, lines 66-67 and column 12, lines 1-2 and 6-11; addresses claims 41, 44 and 49). The ratio of penetration enhancer to active ingredient may vary considerably and will be governed as much as anything, by the pharmacological results that are required to be achieved. In principle, it is desirable that as little absorption enhancer as possible is used (see column 12, lines 26-30; addresses claims 41, 44 and 49). The method may be applied to treat any appropriate disease or

condition (see column 15, lines 38-39; addresses claims 32, 33, 45 and 46). Figure 9 shows the predicted testosterone plasma concentration in hypogonadal males after once daily dosing to steady state with a metered dose (see column 16, lines 37-40; addresses claims 45, 47 and 50)

Reed et al. does not specifically teach a method for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction (claim 32), carbopol, or the specific amounts of the testosterone, isopropyl myristate, carbopol, and ethanol (claims 41, 44 and 49).

Dittgen et al. teach a transdermal therapeutic system for application to the skin and/or mucosa consisting of at least one active substance such as testosterone in amounts of 0.5%, 0.50 g (column 10, lines 1 and 7), or 8.4 mg (see column 12, line 16) in combination with at least one destructing agent and/or at least one structuring agent in a common matrix (see abstract). The composition also comprises a penetration enhancer such as oleic acid and isopropyl myristate from the region of 0 to 1.4% or at least 2% (see column 7, lines 6-8, 41 and 42), carbopol in an amount of 0.5 g and ethanol in an amount of 46.87 g (see column 10, lines 8 and 10).

Kim et al. teaches that the control of the rate and extent of membrane penetration and degree of metabolic conversion is achieved by selecting a vehicle comprising the appropriate polar organic solvent and metabolism modulator, and

varying the proportion of polar organic solvent and metabolism modulator in the vehicle. Thus, for example, control of the rate and extent of membrane penetration and degree of metabolic conversion is achieved by employing isoproyl myristate and ethanol (see column 2, lines 40-45 and column 9, lines 35-37). A greater efficacy of inocoterone acetate when applied in the isopropyl myristate-ethanol mixture was observed and was consistent with the increased transcutaneous penetration observed (see column 9, lines 35-37 and Example 3). The transdermal composition of Kim et al. also comprises carbopol as a viscosity-increasing agents at 0.7 wt/wt (see column 4, lines 29 and 31; example 12).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine Reed et al. and the specific method for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction because first, Reed et al. teach drugs that treat erectile dysfunction. Second, Reed et al. teaches that a lack of efficacy of systemic drugs because of the low drug flux across the skin (see column 1, lines 28-31), and transdermal systemic drug delivery provides an effective method of achieving improved bioavailability for physiologically active substances (see column 1, lines 48-51). Third, Kim et al. teach that a greater efficacy of inocoterone acetate when applied in the isopropyl myristate-ethanol mixture was observed and was consistent with the increased transcutaneous penetration observed (see (see column 9, lines 35-37 and Example 3). Thus, by delivering the drug through a drug delivery system of

Reed et al., and the specific penetration enhancers isopropyl myristate and ethanol will increase penetration of the drug through the skin and thus improve the efficacy.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine Reed et al. and carbopol is because of the following teachings: 1) Reed et al., Dittgen et al. and Kim et al. all teach transdermal pharmaceutical formulations that all contain penetration enhancers; 2) Dittgen et al. teach carbopol in an amount of 0.5 g (see column 10, lines 8 and 10); 3) Kim et al. teach carbopol as a viscosity-increasing agents at 0.7 wt/wt (see column 4, lines 29 and 31; example 12); and 4) "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992); and *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987). Thus, one skilled in the art would be motivated to add carbopol to the composition of Reed et al. because it has been shown in the art that carbopol is used in other transdermal applications with penetration enhancers.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine Reed et al. and the specific amounts of the

testosterone, isopropyl myristate, carbopol, and ethanol because of the following teachings: 1) Reed et al., Dittgen et al. and Kim et al. all teach transdermal pharmaceutical formulations that all contain penetration enhancers; 2) Dittgen et al. teach testosterone in amounts of 0.5%, 0.50 g (column 10, lines 1 and 7), or 8.4 mg (see column 12, line 16), penetration enhancer such as oleic acid and isopropyl myristate from the region of 0 to 1.4% or at least 2% (see column 7, lines 6-8, 41 and 42), carbopol in an amount of 0.5 g and ethanol in an amount of 46.87 g (see column 10, lines 8 and 10); 3) Kim et al. teach carbopol as a viscosity-increasing agents at 0.7 wt/wt (see column 4, lines 29 and 31; example 12); 4) Reed et al. teach isopropyl myristate and ethanol may be used in range of 1 to 50%; 5) Reed et al. also teach that because of the effect of the penetration enhancer, the dosage of the physiologically active agent may often be less than that conventionally used; the concentration of physiologically active agents used in the drug delivery system will depend on its properties and may be equivalent to that normally utilized for the particular agent in conventional formulations; and both the amount of the physiologically active agent and the amount of penetration enhancer will be influenced by the type of effect desired (see column 11, lines 66-67 and column 12, lines 1-2 and 6-11); 6) Reed et al. also teach that the ratio of penetration enhancer to active ingredient may vary considerably and will be governed as much as anything, by the pharmacological results that are required to be achieved; and in principle, it is desirable that as little absorption enhancer as possible is used (see column 12, lines 26-30); 7) It is the normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to

determine where in a disclosed set of percentage ranges is the optimum combination of percentages. See In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980) ("[D]iscovery of an optimum value of the result effective variable in a known process is ordinarily within the skill of the art." See, e.g., In re Baird, 16 F.3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). *In re Paterson* Appeal No. 02-1189 (Fed. Cir. January 8, 2003). Thus, one skilled in the art would be able to adjust the ranges of testosterone, isopropyl myristate, carbopol, and ethanol because of the different amounts provided in prior art such as Reed et al., Dittgen et al. and Kim et al. to achieve the desired pharmacological results.

(2) Claims 33 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reed et al. (US 6,299,900 B1) in view of Dittgen et al. (US 6,238,284 B1), in further view of Kim et al. (US 5,482,970) as applied to claims 32, 37-45, 47 and 50 above, in further view of Wang et al. (Journal of Clinical Endocrinology and Metabolism, August 1998, vol. 83(8), pp. 2749-2757).

The teachings of Reed et al., Dittgen et al. and Kim et al. are as applied to claims 32, 37-45, 47 and 50.

Reed et al., Dittgen et al. and Kim et al. do not teach wherein the subject is eugonadal and wherein the delivery comprises administering the composition to the

right/left upper arms/shoulders and to the right/left sides of the abdomen once per day on alternate days.

Wang et al. teach comparative pharmacokinetics of three doses of percutaneous dihydrotestosterone (DHT) gel in men (see title). The DHT was administered daily over one upper arm; both arms and shoulders; and bilateral arms, shoulders and upper abdomen (see abstract, lines 3-6; addresses claim 48). The serum DHT was maintained at stable levels both in hypogonadal and egonadal men (see page 2750, column 1, lines 1-2; addresses claim 33).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Reed et al., in view of Dittgen et al., in further view of Kim et al. and wherein the subject is eugonadal because Wang et al. teaches that transdermal applications of a testosterone derivative was effective in maintaining stable levels of serum DHT in eugonadal men. Thus, one would be motivated to combine the method of Reed et al. with eugonadal men because of the expectation of success that the penetration enhancers would increase the efficacy of the drug as taught by Reed et al. and Kim et al. Additionally, Reed et al. teach that the method may be applied to treat any appropriate disease or condition (see column 15, lines 38-39).

(3) Claims 34 and 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Reed et al. (US 6,299,900 B1) in view of Dittgen et al. (US 6,238,284 B1), in further view of Kim et al. (US 5,482,970) as applied to claims 32, 37-45, 47 and 50 above, in further view of Doherty, Jr. et al. (US 6,037,346)

The teachings of Reed et al., Dittgen et al. and Kim et al. are as applied to claims 32, 37-45, 47 and 50.

Reed et al., Dittgen et al. and Kim et al. do not teach a phosphodiesterase type 5 inhibitor or VIAGRA, UPRIMA, TRENTAL or ACTIBINE.

Doherty, Jr. et al. teach local administration of phosphodiesterase inhibitors, preferably type V (see column 3, lines 66-67) for the treatment of erectile dysfunction (see title; addresses claim 34). The drug is delivered transdermally, which includes percutaneous administration (see column 4, line 60 and column 6, lines 22-23). Various compounds are known as inhibitors of phosphodiesterases including sildenafil citrate (VIAGRA; see column 3, lines 21-22 and 25; addresses claim 36)

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Reed et al., in view of Dittgen et al., in further view of Kim et al. and a phosphodiesterase type 5 inhibitor or VIAGRA is because Doherty, Jr. et al. teach percutaneous administration of phosphodiesterase

type 5 inhibitor such as VIAGRA for the treatment of erectile dysfunction (see column 3, lines 21-22 and 25 and title). Thus, one would be motivated to combine the method of Reed et al. with eugonadal men because of the expectation of success that the penetration enhancers would increase the efficacy of the drug as taught by Reed et al. and Kim et al.

(4) Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Reed et al. (US 6,299,900 B1) in view of Dittgen et al. (US 6,238,284 B1), in further view of Kim et al. (US 5,482,970) as applied to claims 32, 37-45, 47 and 50 above, in further view of Dobs et al. (The Journal of Clinical Endocrinology and Metabolism, October 1999, vol. 84(10), pp. 3469-3478)

The teachings of Reed et al., Dittgen et al. and Kim et al. are as applied to claims 32, 37-45, 47 and 50.

Reed et al., Dittgen et al. and Kim et al. do not teach wherein the man suffers from primary hypogonadism.

Dobs et al. teach pharmacokinetics, efficacy and safety of a permeation-enhance testosterone transdermal system (TDD) in comparison with bi-weekly injections of testosterone enanthate for the treatment of hypogonadal men (see title). Both

treatments are efficacious for replacing testosterone in hypogonadal men, the more physiological sex hormone levels and profiles associated with TDD may offer possible advantages over intramuscular injections (see abstract, column 2, last paragraph). Out of the 33 male patients treated, 10 or 30.3 % were primary hypogonadal and 23 or 69.7% were secondary hypogonadal (see page 3471, table 1).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Reed et al., in view of Dittgen et al., in further view of Kim et al. and wherein the subject is eugonadal because Dobs et al. teaches that transdermal applications have more advantages then injections of testosterone for the treatment of primary hypogonadal men (see abstract, column 2, last paragraph and see page 3471, table 1). Thus, one would be motivated to combine the method of Reed et al. with eugonadal men because of the expectation of success that the penetration enhancers would increase the efficacy of the drug as taught by Reed et al. and Kim et al. Additionally, Reed et al. teach that the method may be applied to treat any appropriate disease or condition (see column 15, lines 38-39), and showed the predicted testosterone plasma concentration in hypogonadal males after once daily dosing to steady state with a metered dose (see column 16, lines 37-40 and Figure 9).

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kendra D. Carter whose telephone number is (571) 272-9034. The examiner can normally be reached on 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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